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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,335	06/13/2001	Hermann-Joseph Grone	P/717-189	9473

1444 7590 10/22/2002

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EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/22/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/787,335	Grone et al.
Examiner	**Art Unit**
Fozia Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 22, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-22 and 24-36* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-22 and 24-36* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Receipt of Applicants' amendment canceling claims 23 and 34 and amending claims 24 and 35, filed on 22 July 2002, in Paper No.13 is acknowledged.

Thus claims 17-22, 24-33, 35-37 are pending and under consideration by the Examiner.

2. The following previous rejections and objections are withdrawn in light of Applicants amendments filed in Paper No.9, 06/24/02:

(i) The objection to the specification for not containing a reference to the priority Applications.

(ii) The rejection of claims 17-19, 21-30, 32-37 made under 35 U.S.C. 103(a) as being unpatentable over Pattison et al (1994) in view of Proudfoot et al. (1996) and further in view of Matindale (1996) is withdrawn, because Applicnats arguments that there is no suggestion or motivation, in any of the applied references to combine cyclosporin and the chemokine receptor antagonist, Met-Rantes, (two separate immunisuppressive immunomodulating agents), is persuasive. Also Applicants showed that cyclosporin and Met-Rantes worked synergistically together and unexpectedly reduced nephrotoxicity of cyclosporin, which is the major side effect of this potent immunosuppressive drug.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim rejections-35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 17-22, 24-33, 35-37 stand rejected under 35 U.S.C. § 112, first paragraph, for reasons of record set forth in the office action mailed on 21 February 20, in Paper No:10, pages 2-6.

Applicants argue that cyclosporin A is a commercially available drug which has attained widespread clinical application as an immunosuppressant in organ transplantation without any specificity towards any particular organ, and Met-RANTES has recently been shown to give good results in animal models of intestine transplant and improves acute-rejection induced microvascular injury in rat small bowel transplantation. Furthermore, Met-RANTES has the unexpected property of reducing the nephrotoxicity of cyclosporin, thus both Cyclosporin and Met-RANTES show activity in treating or preventing transplant rejection.

With respect to the breadth of the chemokine receptor antagonist, Applicants argue that Met-RANTES is only one example of an antagonist of the chemokine receptors for RANTES, and that the specification discloses other chemokine receptor antagonists, for which RANTES and N-terminally extended RANTES are among them. Thus Applicants contend that given the guidance that the N-terminus can be modified to produce RANTES antagonist, and that truncated or N-terminally extended RANTES are already disclosed in the art, it would take only routine experimentation to find other antagonists of the chemokine receptor of RANTES. Finally, Applicants point out that chemokines are among the most widely studied class of proteins and are known to be involved in a variety of diseases, and that there are many chemokine antagonists that modulate the action of chemokines at the sites of inflammation. Modification of N-terminus produces strong antagonists together.

Applicants arguments have been fully considered and are deemed persuasive in part. Applicants' first argument that both Cyclosporin and Met-RANTES show activity in treating or preventing transplant rejection, is persuasive. Thus, instant specification provides reasonable enablement for a method of treating or preventing the rejection of transplanted organs, tissues or cells by administering a pharmaceutical composition comprising the antagonist Met-RANTES and Cyclosporin, and a pharmaceutical composition comprising Met-RANTES and cyclosporin.

With respect to Applicants' second argument, a method of treating or preventing the rejection of transplanted organs by antagonizing all chemokine receptors is still not enabled by instant specification. While antagonizing RANTES receptor and producing other antagonists of the chemokine receptor of RANTES, to treat or prevent the rejection of transplanted organs, is enabled, a method of treating or preventing organ transplant rejection, by administering a pharmaceutical composition comprising "all possible" chemokine receptor antagonists and Cyclosporin or a pharmaceutical composition comprising "all possible" chemokine receptor antagonists and Cyclosporin, is not enabled. The only chemokine receptor disclosed in the instant specification to play a role in the rejection of organ transplant is RANTES receptor. Therefore, the issue is not whether or not the skilled artisan can produce chemokine antagonists. However, the physiological effects of chemokine receptors and their agonists are diverse (see Elias et al. Structure, Function and Inhibition of Chemokines, Annual Review of pharmacology and Toxicology, 2002, Vol. 42, pages 469-499, especially page 479-487), and one of ordinary skill in the art would not expect antagonizing chemokine receptors other than the receptor for RANTES, would result in the reduction of graft

rejection or would work synergistically with cyclosporin to reduce nephrotoxicity induced by cyclosporin.

Therefore, instant specification is only enabling for a method of treating or preventing the rejection of organ transplantation by administering a pharmaceutical composition comprising an antagonist for the RANTES receptor, in combination with Cyclosporin and a pharmaceutical composition comprising antagonist for the chemokine receptor RANTES and Cyclosporin.

Conclusion

5. No claim is allowed, however, claims 21-22 and 32-33 would be allowable if rewritten in an independent format, to overcome the rejection(s) under 35 U.S.C. 112, first paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Art Unit: 1647

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
08 October 2002

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